

Influence of body position on crossed-spinal excitability in
high-risk fallers

by

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Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirements
for the degree
Master of Sciences
in the Department of Kinesiology of
Indiana University
September 2015

Accepted by the Graduate Faculty, Indiana University, in partial fulfillment of the requirements for the degree Master of Science.

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September 9, 2015

Abstract

The purpose of this study was to examine the role body position plays on crossed-spinal excitability in high-risk fallers. Specifically, we examined the time-course modulation of the soleus H-reflex following a conditioning stimulation from the contralateral common peroneal nerve in high-risk fallers. Four high-risk fallers (72.65 ± 5.22 years) volunteered to participate in this study. Two body positions were studied: supine and standing. A conditioning stimulus was given to the contralateral common peroneal nerve of the left leg followed by a test stimulus at varying interstimulus intervals (25-300ms) to the ipsilateral tibial nerve of the right leg to elicit a soleus H-reflex. Surface EMG electrodes were used to record EMG activity of the left tibialis anterior and right soleus muscles. The peak-to-peak amplitude of the soleus H-reflex was recorded ten times at each ISI and control (unconditioned) stimulations to the soleus muscle. The highest and lowest values at each ISI were removed and the remaining 8 peak-to-peak amplitudes were averaged. For all calculations, the alpha level was set at the .05 level. A 2 x 6 ANOVA (body position by interval) revealed no significance interaction $F_{(5, 15)} = 0.23$, $p = 0.93$. Similarly there was no significant main effect for body position $F_{(1, 15)} = 0.178$, $p = 0.702$ or interval $F_{(5, 15)} = 0.29$, $p = 0.319$. A post hoc power analysis was conducted using G-Power. This analysis indicated

that approximately 8-14 subjects would be needed to detect significant differences in reflex modulation in high-risk fallers at the 0.05 level of significance.

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Chapter 1

Introduction

As the population continues to age, one of the most significant problems faced is a decrease in the quality of life. This reduction in quality of life is likely associated with increases in functional limitations and chronic disease. Functional limitations such as walking, grasping, carrying, and pushing had a prevalence rate of 51.8% in people over the age of 65 years (Brault, Hootman, Helmick, Theis, & Armour, 2009). Additionally, the leading cause of injury related deaths in people over the age of 65 were fall-related injuries (CDC, 2009). Since the over 65 age-group is the fastest growing age group in our nation, comprising 15-20 percent of Americans, falls and fall-related deaths will only become more common as this trend continues due to longer lifespans and access to better medical care. Much of the current literatures' focus has primarily been on the role that physical activity plays in cognitive and executive functioning (Hillman, Erickson, & Kramer, 2008). Most current research focuses primarily on cortical functions and pays little attention to subcortical regions and spinal cord function. The central nervous systems high degree of connectedness is due to a multitude of

interconnected circuits, of which the spinal cord is part of and required for normal motor function and daily living. The maintenance of all neural circuits, including spinal circuitry, is essential in reducing functional limitations in the aging population.

The spinal cord plays an important role in healthy living by incorporating both descending inputs from higher levels of processing and by integrating sensory inputs to produce specific patterns of muscle activation across sides of the spinal cord. However, the aging of the spinal motor system is marked by several neurological changes including but not limited to, decreased nerve conduction velocity (Brooke, Singh, Wilson, Yoon, & McIlroy, 1989), sensory and motoneuron loss (Flanigan, Lauria, Griffin, & Kuncl, 2002), decreased maximal motor unit discharge rates (Kamen & Knight, 2004), and depressed reflex responses (Koceja, Markus, & Trimble, 1995). All of which can have profound effects on motor performance.

Despite there being a loss in the number of motoneurons, the remaining motoneurons are still subject to modifications such as the reshaping of dendritic tree size and decrease in synaptic input (Edström et al., 2007). Much like the morphological changes the remaining motoneurons can undergo, the spinal interneurons too can be modified during the aging process. Little work has been done in investigating the

morphological changes spinal interneurons undergo, despite the critical role spinal interneurons play in coordinating motor performance by processing and relaying information from supraspinal and sensory inputs. Age related morphological changes of the interneurons are a potential source of impeded coordination and reflex deficits. The loss of neurons in the spinal cord as aging occurs results in a decrease in the neural control of muscles, and thus, a decrease in the amount postural control one has.

A very important spinal reflex that has shown a high degree of modification during the aging process is the spinal stretch reflex. The spinal stretch reflex serves as a component of proprioception, relaying muscle length information to the CNS. The change in muscle length is detected by specialized sensory receptors called muscle spindles located in the belly of the muscle. This stretch information is sent to the spinal cord via Ia afferents that make a monosynaptic connection to alpha motoneurons. The alpha motoneurons synapsed with are the same ones that innervate the muscle containing the stimulated spindles. Since this is a monosynaptic connection, information can be received and sent very fast; thus, allowing the CNS to monitor muscle length and force (Houk, 1976). A deficit in the spinal stretch reflex could result in an increased risk for injury in elderly populations due to slower than normal response

time. In elderly subjects, a reduction in the spinal stretch reflex and the H-reflex amplitude, along with a lack in the ability to modulate these reflexes has been demonstrated in several studies (Koceja & Mynark, 2000; Morita et al., 1995; Mynark, 2005). When young subjects moved from a prone, non-weight bearing position to a standing, weight bearing position they depressed their H-reflex; whereas, elderly subjects maintained the same H-reflex amplitude regardless of body position (Koceja et al., 1995). This illustrates that elderly subjects are not able to modify their neural responses to a changing environment in the same way young subjects were.

Ipsilateral sensory information from one limb has been the main focus of research in regards to aging spinal reflexes. While sensory information does provide an important aspect to the synergistic combination of the motor and sensory systems in the spinal cord, the spinal stretch reflex is also capable of modulation across joints. This is an essential function for the muscle coordination and postural control between the right and left sides of the body during bilateral movements such as locomotion. Sherrington (1910) first demonstrated the importance of crossed-spinal modulation by evoking a flexion reflex in a limb and observing an extension reflex in the contralateral limb. Additionally, Grillner (1981) showed that spinalized cats' spinal cords alone are able to modulate each limb's walking

speed independently of the other. This ability of each limb to be modulated independently shows that the spinal cord must contain circuits that allow for contralateral coordination to occur without input from supraspinal areas.

One method for testing crossed-spinal reflexes in a human is to use a Ia conditioning stimulus to the contralateral limb followed by an elicitation of the H-reflex to ipsilateral, test limb. With a conditioning stimulus proceeding the test stimulus between 3-33ms to the ipsilateral tibial nerve resulted in an inhibition of the soleus H-reflex in the contralateral limb (Peter W Stubbs, Nielsen, Sinkjær, & Mrachacz-Kersting, 2011).

With an interstimulus delay of such a short time, 3-33ms, producing an inhibition in the contralateral limb indicates that the response is being modulated at the spinal cord level and not at supraspinal areas of higher processing. In addition to short interstimulus intervals, longer intervals ranging from 0-300ms have also been examined by Kamen and Koceja (1989). By varying the interstimulus interval, it was found that young subjects demonstrate an inhibition of the test muscle when the contralateral conditioning stimulus' arrival falls between 0-50ms prior to the ipsilateral test H-reflex; facilitation of the test H-reflex is observed at longer conditioning intervals between 60-200 ms. Differing substantially from young subjects

at both short and long conditioning intervals, elderly subjects showed an exaggerated response of greater inhibition at lower interstimulus intervals and greater facilitation at longer interstimulus intervals (Figure 1). Elderly subjects' peak facilitation is shifted from approximately 75ms, as observed in young subjects, to 150ms.

This over-exaggerated response of inhibition and facilitation in elderly crossed-spinal reflex modulation, due to information from the opposing limb, could contribute to deficits in interlimb coordination and perhaps an increase in postural instability as a result of decreased crossed-spinal communication. Rarely studies investigations have focused on the modulation and plasticity of the crossed-spinal pathways in the elderly and none have examined the crossed-spinal reflexes in high-risk fallers.

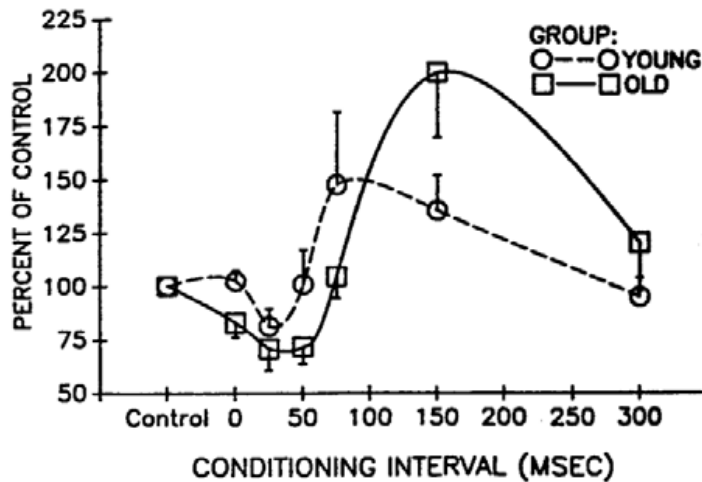


Figure 1. Asymmetry in crossed-spinal reflexes in the elderly.

Peak reflex force following a conditioning tendon tap in the contralateral limb. Reflex force is represented as a percentage of the control reflex. Elderly subjects show larger deviations from 100% compared to the young. Also, there is a shift in peak facilitation in the old group from approximately 75ms in young subjects to 150ms in old subjects. From Kamen and Koceja (1989).

The majority of research regarding falls in elderly populations has focused on the biomechanical aspects of slipping and tripping along with the voluntary recovery from postural perturbations (Tang & Woollacott, 1998; Troy & Grabiner, 2006; Van den Bogert, Pavol, & Grabiner, 2002). Van den Bogert and colleagues demonstrated that one of the most valuable variables in falls is the response time (Van den Bogert et al., 2002); furthermore, Owings and colleagues showed that reaction time between the failed attempt and a successful attempt at recovery lies within a window of just 40-50ms (Owings, Pavol, & Grabiner, 2001). With such a short amount of time, 10ms, making the difference between a successful recovery from perturbation and a

failed recovery, it stands to reason that the spinal circuitry's health and viability play a role in one's ability to adequately maintain a stable upright position.

Purpose of Research

The purpose of this research is to examine the role body position plays on crossed-spinal excitability in high-risk fallers. Specifically, it will examine the time-course modulation of the soleus H-reflex following a conditioning stimulation from the contralateral common peroneal nerve in high-risk fallers.

Chapter 2

Review of Literature

The purpose of this research is to examine the role body position has on crossed-spinal excitability in high-risk fallers. Specifically, it will examine the time-course modulation of the soleus H-reflex following a conditioning stimulation from the contralateral common peroneal nerve in high-risk fallers. This chapter will be divided in the following way: 1) Spinal Stretch Reflex and H-reflex; 2) H-reflex Plasticity and Modulation; and 3) Summary.

Spinal Stretch Reflex and H-reflex

Charles Sherrington was the first to explore spinal stretch reflexes, starting in the early 20th century. While studying decerebrate cats, it was noticed that when hind limb muscles were passively stretched, the stretched muscle exhibited an increased contraction (Sherrington, 1906). Given that the cat had been decerebrated, and therefore, the spinal cord was acting in isolation from supraspinal areas, Sherrington concluded that the passive stretch information had the ability to create excitation in the homonymous motoneurons, which resulted in the observed contraction of the stretched muscle. Since it was first described, much work has been done on understanding the underlying mechanisms of the spinal stretch reflex (SSR).

Within a muscle's extrafusal fibers there are highly specialized sensory receptors called muscle spindles. The extrafusal fibers are the force generating muscle fibers while the intrafusal fibers, a component of the muscle spindle that serve to monitor muscle length but provide no force, are embedded in parallel with the extrafusal fibers. Muscle spindles are approximately 4-10mm in length and have a variety of morphological differences within a species from muscle to muscle and across species alike (Burke & Gandevia, 2012). The density of muscle spindles within a muscle seems to be dependent on the function of that muscle. For example, a large muscle such as the

quadriceps femoris has over 1300 spindles while small intrinsic muscles of the hand have been found to have fewer than 50, so while the large muscles may have a greater number of spindles, the density of muscle spindles is likely to be higher in intrinsic muscles of the hands and neck (Burke & Gandevia, 2012; Prochazka & Hulliger, 1982). A muscle spindle is composed of three components: 1) intrafusal fibers 2) primary and secondary sensory endings and 3) gamma motor endings (E. R. Kandel, Schwartz, & Jessell, 2000). Intrafusal fibers can be subdivided into three types: dynamic nuclear bag fibers, static nuclear bag fibers, and nuclear chain fibers. Primary sensory endings are found wrapped around the middle aspect of all three fiber types while the secondary sensory endings are located distal to the primary endings on static nuclear bag and chain fibers. Primary sensory endings join together once they exit the muscle spindle and form a single Ia afferent fiber. Secondary sensory endings make multiple group II fibers once outside the muscle spindle. Each type of sensory ending within the muscle spindle is sensitive to different types of stimuli. Primary sensory endings respond to dynamic and static changes in muscle length, as well as vibrations. The secondary sensory endings also respond to static length changes, but not dynamic length changes or vibrations (Pierrot-Deseilligny & Burke, 2005). At the end of the muscle spindle are two types of small diameter gamma

motoneurons, static and dynamic. The role of static gamma motoneurons is to modulate nuclear chain and static nuclear bag fibers while that of dynamic gamma motoneurons is to act on dynamic nuclear bag fibers. Regardless of the gamma motoneuron type, when they are activated they contract, stretching the central portion of the muscle spindle since they are located distally. The change in length is then sensed by the primary and secondary endings wrapped around the muscle spindle fibers. The role of the gamma motoneurons is to keep the intrafusal fibers taut. The CNS has the ability to adjust the tautness of the nuclear bag and chain fibers by way of the gamma motoneurons. Figure 2 depicts the anatomy of a muscle spindle.

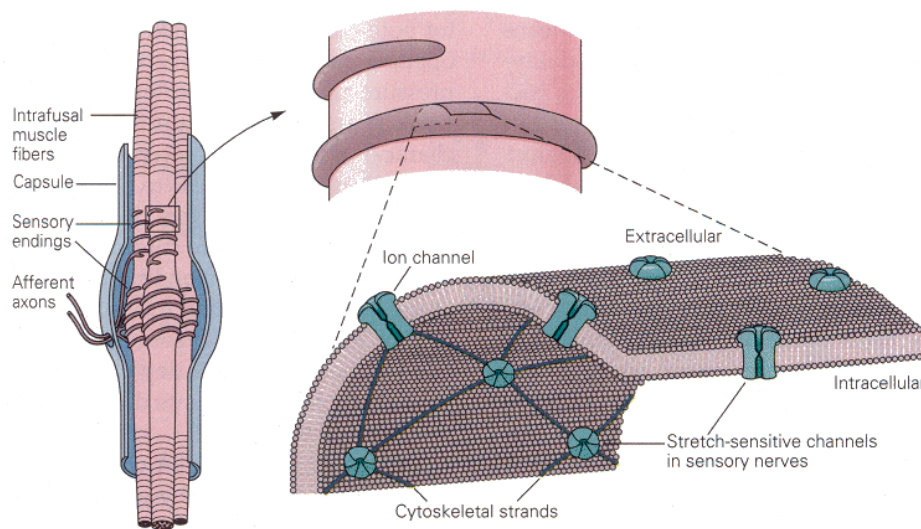


Figure 2. Muscle spindle anatomy. Showing intrafusal nuclear bag and chain fibers with sensory endings wrapped around them. Also depicted is an enlarged section of the sensory axon membrane complete with ion channels. (E. Kandel, Schwartz, J., 2000).

The H-reflex, or Hoffmann reflex, first described by Paul Hoffmann in the early 20th century (Hoffmann, 1910, 1918) is a monosynaptic reflex much like a mechanically induced spinal stretch reflex (P. E. Zehr, 2002); however, by bypassing the muscle spindle, the H-reflex can be a useful tool in accessing the modulation of these monosynaptic connections (Palmieri, Ingersoll, & Hoffman, 2004).

To elicit the H-reflex, an electrical pulse is delivered to a mixed nerve, containing both afferent (sensory) and efferent (motor) fibers. The afferent fibers transmit the stimulus to the spinal cord where it synapses with the α -motoneuron. It is the α -motoneurons that then travel from the spinal cord to the muscle and form part of the neuromuscular junction. With an adequate amount of stimulation, this reflex arc results in the "H-reflex". Additionally, the stimulus results in the direct stimulation of the muscle (from the site of stimulation to the neuromuscular junction). This direct stimulation results in the "M-wave". Figure 3 A & B depict a simple schematic of the neural circuitry involved in eliciting a M-wave and H-reflex (A); as well as an EMG trace depicting both the M- and H-waves (B). The time differences in which the M-wave and H-reflex appear are a result of the distance the stimulus travels and the addition of synapsing as is the case in the H-reflex. At lower levels of

stimulus intensity only the H-reflex will be evoked but at higher levels of stimulus intensity an M wave will appear.

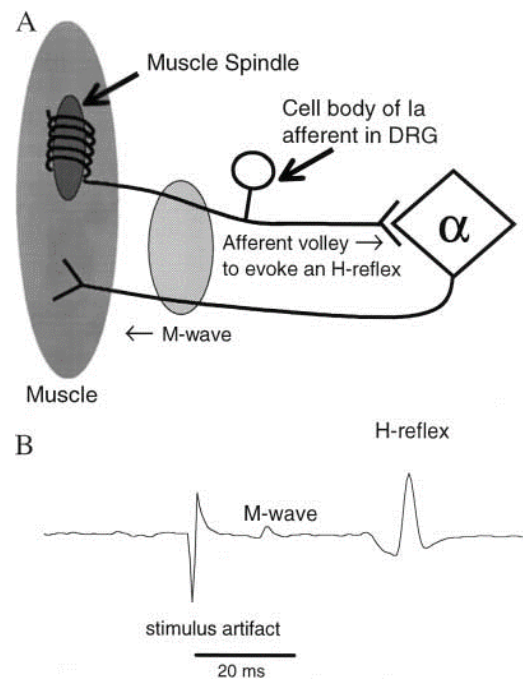


Figure 3. Monosynaptic H-reflex pathway and EMG trace. **A:** Schematic of the spinal pathway for a monosynaptic H-reflex. The stimulation of the mixed nerve is depicted by the grey ellipse. From the stimulation site, the impulse travels orthodromically from the α -motoneuron to produce the M-wave, and orthodromically in the Ia (sensory) fiber to produce the H-reflex. **B:** Averaged H-reflexes ($n=20$) from the soleus with a tonic 10% MVC contraction. Figure taken from Zehr 2002. Data (2B) from Zehr and Stein, 1999.

In bypassing the muscle spindle, yet still achieving the desired activation of the motoneuron pool, the H-reflex has been able to provide useful insight into sensorimotor integration and spinal cord plasticity and modulation.

H-reflex Modulation and Plasticity

H-reflex methodology has been used to investigate the effects of training on spinal cord plasticity in humans (Palmieri et al., 2004), mice (P. E. Zehr, 2002), and non-human primates (Hoffmann, 1910). The training induced changes, mediated at supra- and local spinal levels, appears to have an influential role in shaping the plastic and modulatory properties of the H-reflex as well as the spinal stretch reflex when acquiring and maintaining novel motor skills. The H-reflex has often been used as a means to study spinal cord plasticity (Wolpaw & Tennissen, 2001). Since the H-reflex can be influenced at various areas in the CNS, several techniques have been developed in which to assess plastic and modulatory changes of the spinal reflex. Some of the important techniques will be discussed below.

Motoneuron Plasticity

One component of the CNS that has shown plasticity is the α -motoneurons involved in the spinal stretch and H-reflex circuits. This idea that the reflex circuit could be a source of plasticity began with an operant conditioning study in 1989 by Wolpaw and Lee (Wolpaw & Lee, 1989). For operant conditioning to occur, associations must be made between a behavior or action and a consequence of that behavior (E. R. Kandel et al., 2000).

Wolpaw and Lee (1989) rewarded monkeys when they either up-trained the H-reflex or down-trained the H-reflex with 3,000-6,000 trials per day for up to 6 months. Post-training, the monkeys could successfully up- or down-train their reflex response. This effect was observable three days post spinal cord transection, even with the presence of pentobarbital, which acts strongly in depressing spontaneous interneuronal activity. These results led to the idea that the site of plasticity could be the H-reflex circuitry itself and began numerous studies that further examined potential mechanisms that could play a role in these plastic changes. Since the original study in 1989, the following changes have been observed in animals capable of operant down-training their H-reflex, compared to those that failed in training the reflex: 1) a positive shift in the motoneuron firing threshold and 2) a decrease in conduction velocity (Carp & Wolpaw, 1994). A potential source for the decreased H-reflex after conditioning is the greater depolarization needed for the motoneuron to reach threshold, as well as the associated EPSPs. The change in the motoneuron firing threshold and reduced conduction velocity has been proposed to be a result of a positive shift in the Na^+ channel voltage dependence (Halter, Carp, & Wolpaw, 1995). Animals that were successful in the down-conditioning of the H-reflex were also discovered to have an increased number of GABAergic terminals on

the motoneurons involved in the conditioned pathway (Wang, Pillai, Wolpaw, & Chen, 2006), and an increase in the number of inhibitory GABAergic interneurons in the spinal cord ventral horn (Wang, Pillai, Wolpaw, & Chen, 2009), compared to animals that were unable to successfully down-condition the H-reflex. However, up-conditioning of the H-reflex has not shown opposite effects of down-conditioning and changes in the up-conditioned animals have yet to be detected (Carp & Wolpaw, 1995).

Post-Activation Depression

A requirement for normal movement is the ability of the motor system to modulate input from Ia afferents onto the motoneurons they synapse with. A mechanism that appears to play a role in modulating the synaptic transfer of information from Ia afferent fibers and the motoneurons is the past activation history of the Ia afferents. Ia afferent activation in close succession causes a depression in synaptic transmission between the Ia afferents and motoneurons with which it projects to, which is known as post-activation depression. The depressive effects of the previously activated are long-lasting, greater than 10s of the monosynaptic stretch reflex and H-reflex (Hultborn et al., 1996) It is thought that the long-lasting depression occurs at the Ia afferent axon terminal.

Post-activation depression is accessed in humans using two methodologies: 1) Passive stretch of the test muscle prior to eliciting the H-reflex and 2) Paired reflex stimuli to homonymous nerve. In the first method, it has been shown that the passive dorsiflexion of the foot for up to 2s produces a long-lasting depression, up to 10s, in the soleus H-reflex (Hultborn et al., 1996). The second method, known as paired reflex depression, involves delivering a pair of stimuli to a homonymous nerve. The time between the two stimuli is usually 80ms apart, evoking two H-reflexes. The percentage of the second H-reflex compared to the first H-reflex gives a measure of the effects of activation history on the reflex. Trimble and colleagues found subjects depressed the reflex by 73% and more than 78% when standing (Trimble, Du, Brunt, & Thompson, 2000).

Cross-Spinal Conditioning

Stimuli that evoke H-reflex responses do not have to be ipsilaterally located. Sherrington described a contralateral reflex that occurred when a noxious stimulus was applied to the ipsilateral side and caused an ipsilateral flexion withdrawal response (Sherrington, 1910). To further examine the effect of the crossed-spinal reflex arising from Ia afferents of the ipsilateral soleus on the contralateral ankle extensors and flexors, Baxendale and Rosenberg (1976) applied a low amplitude,

high frequency vibration to the ipsilateral soleus tendon in the decerebrated cat. The contralateral soleus and tibialis anterior were isotonicallly weighted and their lengths monitored as a result of the ipsilateral conditioning stimulation. It was found that Ia afferent activation caused a lengthening of both the contralateral soleus and tibialis anterior muscles. Ia afferents project to multiple areas of the CNS, including neurons that cross the spinal cord. It is known that the mid lumbar region of felines comprises commissural interneurons which synapse with the contralateral grey matter motoneurons (Jankowska et al., 2009). While humans display crossed-spinal reflexes, it is still not known what neurons are responsible for these responses. During the aging process, a change in the crossed-spinal reflex is observed. Kamen and Koceja (1989) found in younger subjects, an ipsilateral conditioning tendon tap to the patellar tendon evoked inhibition in the contralateral test muscle at shorter interstimulus intervals (0-50ms) and facilitation of the test muscle at longer intervals (60-200ms). However, older adults showed greater levels of inhibition and facilitation compared to younger subjects as well as a rightward shift of their peak inhibition and facilitation. It seems that during the aging process, crossed-spinal communication becomes impaired (Figure 1).

Summary

The spinal cord incorporates information from several sources such as Ia afferent interneuron pathways, presynaptic modulation of Ia afferents, and sensory input. All of this information is then used to create unilateral and bilateral movements. However, as the human CNS ages, it results in deficits and inappropriate modulation of reflex pathways. These decrements can result in impairments in motor function and the potential of reduced physical activity in later years of life. Additionally, the SSR and the soleus H-reflex have shown deficits in older adults.

Similarly to older adults demonstrating a reduced SSR and H-reflex, they also show inappropriate modulation of crossed-spinal reflexes. Older adults show greater levels of facilitation and inhibition compared to young healthy adults along with a rightward shift to longer interstimulus intervals in these peaks. It does seem clear that these crossed-spinal pathways play an important role in coordinating bilateral movement. It is not known how the crossed-spinal reflex is modulated in a population at high-risk for falling.

Chapter 3

Methodology

The purpose of this research is to examine the role body position has on crossed-spinal excitability in high-risk fallers. Specifically, it examined the time-course modulation of the soleus H-reflex following a conditioning stimulation from the contralateral common peroneal nerve in high-risk fallers. The methods of this study will be presented in the following arrangement: 1) Subject recruitment; 2) Equipment; 3) Experimental procedures; 4) Experimental protocol; and 5) Data Analysis.

Subjects

Four subjects between the ages of 65 and 85 were recruited for this study. Subjects were recruited from one population: high-risk fallers. All subjects were determined to demonstrate an increased risk in incurrence of falls, and therefore, they are classified as "high-risk fallers" by their personal physicians or physical therapists that referred them to this study. All subjects' relevant medical history was collected. Refer to Appendix A for a complete version of the medical questionnaire used. Both sexes were recruited for this study, since no differences between genders has been observed in

literature (Buschbacher, 1999). Subjects who met any of the following criteria were not allowed to take part in the study.

- 1) Body mass index $> 31\text{kgm}^{-2}$
- 2) Uncontrolled hypertension (resting systolic > 170 mmHg, diastolic > 100 mmHg)
- 3) Symptomatic coronary artery disease
- 4) Myocardial infarction in the last 12 months
- 5) Peripheral neuropathy (diabetic and idiopathic)
- 6) Intermittent claudication with symptoms at < 150 m of walking
- 7) Dizziness
- 8) Vertigo
- 9) Cancer - chemotherapy within 6 months
- 10) Pulmonary embolism or thrombophlebitis within 6 months; pulmonary disease requiring chronic O_2

Subjects selected were also required to have a soleus H-reflex that was measurable and recordable as well as a motor response from their tibialis anterior. A lack of any of these three criteria barred subjects not presenting any of the exclusion criteria from participating in this study. Before testing, each subject read and signed the informed consent document, which was approved by the Indiana University Human Subjects Committee. An approval number from the Indiana University Institutional Review Board for this study can be found in Appendix B.

Equipment

To record muscle activity of the lower limb, active bipolar electrodes were placed on the soleus and tibialis anterior muscles of the dominant leg. The signals from the recording electrodes were amplified with a gain of 1000x (Delsys Bagnoli 16-EMG system). For digitization, a WinDag Pro Data Acq™ system was used to record EMG signals and output from the stimulators with sampling rate set at 2000 Hz. Two stimulator types were used for this study: GRASS, S88 model (Astro-Med Inc.) and model DS7A from DIGITIMER Limited. To ensure subjects' safety from unintended electrical shock, a stimulus insulation unit (GRASS, SIU5) and a constant current unit (GRASS, CCU) was connected with GRASS stimulator. A custom Matlab® (MathWorks, Inc.) program was used to calculate the variables from sampled signals of EMG for later analysis.

Experimental Procedures

Electromyography set-up, recording and stimulation

The motor responses (m-waves) and H-reflexes were both recorded using bipolar surface electrodes (Delsys) with 1 cm parallel bars and an interelectrode distance of 1 cm were used and sent through an amplifier (Delsys Bagnoli 16-EMG system) with a gain of 1000x. Electrodes were placed on both lower limbs at locations on the soleus (SOL) and tibialis anterior (TA)

muscles. The SOL electrode placement was on the inferior, posterior lower leg, parallel with the muscle fiber run and just superior to the Achilles tendon. The TA electrode was placed in parallel with the muscle fibers, lateral to the medial shaft of the tibia approximately one-third the distance between the knee and the ankle.

Two sets of stimulating electrodes were used to stimulate the posterior tibial nerve of the right leg and the common peroneal nerve of the left leg (Figure 4). The right leg tibial nerve stimulation was an 8 mm diameter cathode electrode and was placed in the popliteal fossa, and a 4 cm diameter anode electrode was placed just superior to the right patella. The common peroneal stimulation of the left leg used a bipolar electrode with an 8 mm diameter and a 1 cm interelectrode distance, which was placed just distal to the fibular head.

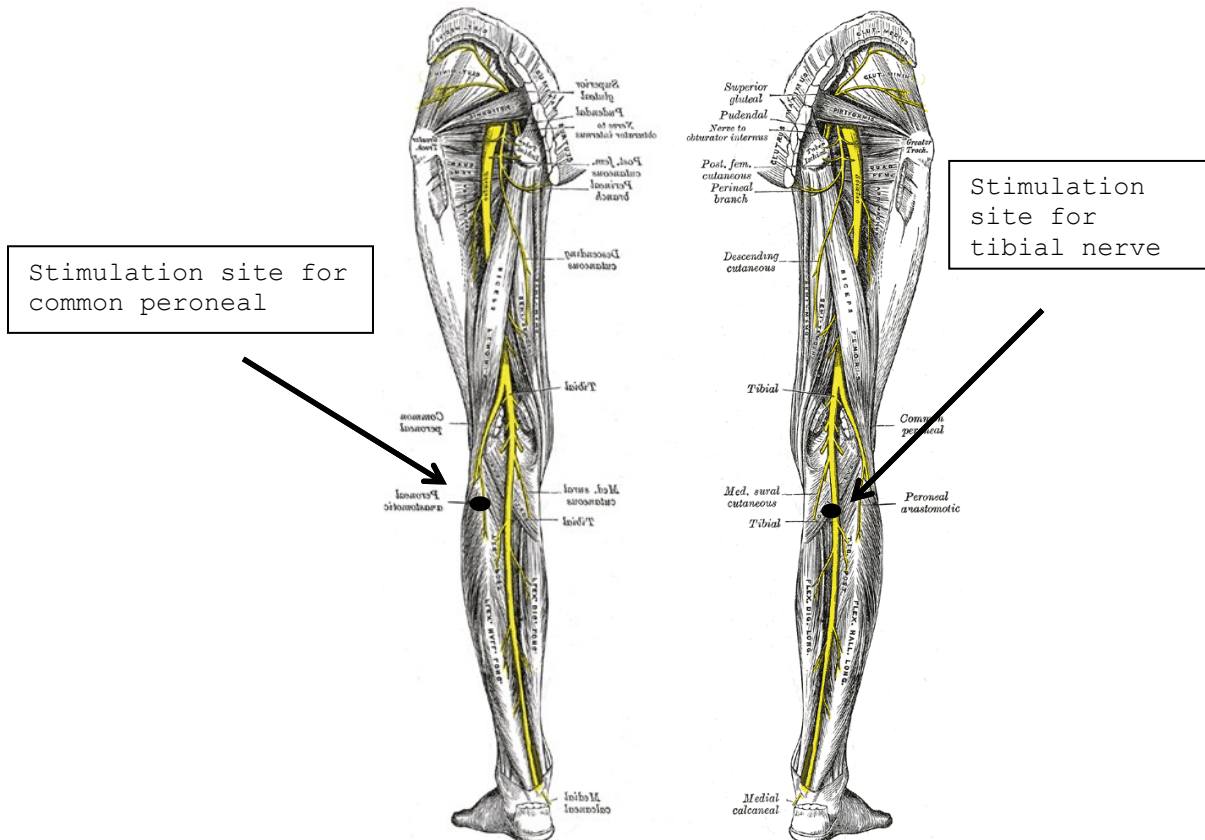
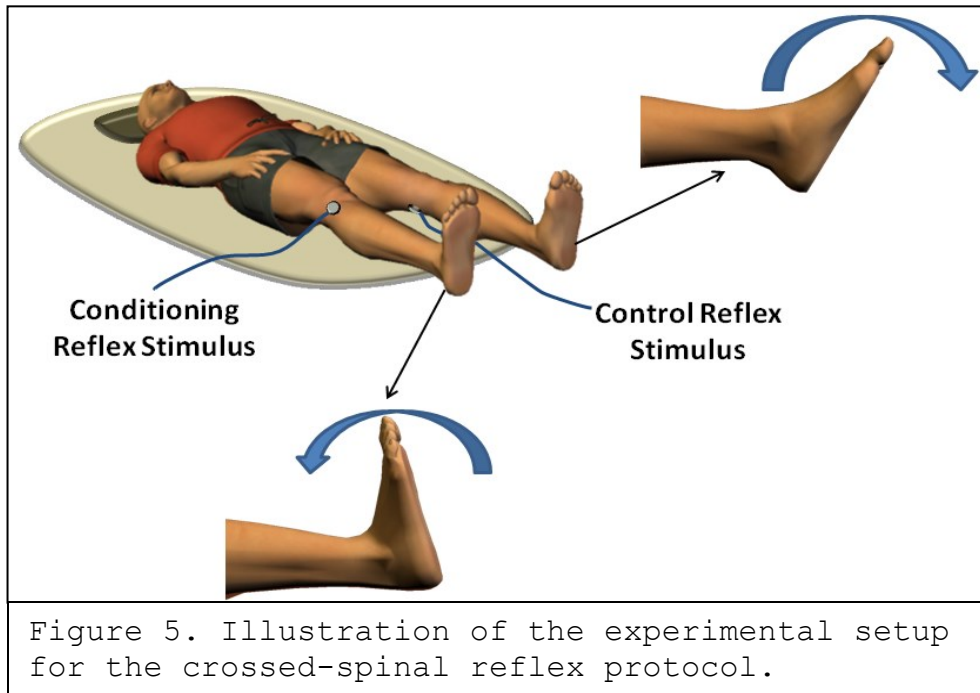


Figure 4. Stimulation sites for crossed-spinal reflex conditioning. Depicting the location of both the tibial nerve and the common peroneal nerve. The black dots represent stimulation sites. The left leg received common peroneal nerve stimulation and the right leg received tibial nerve stimulation.

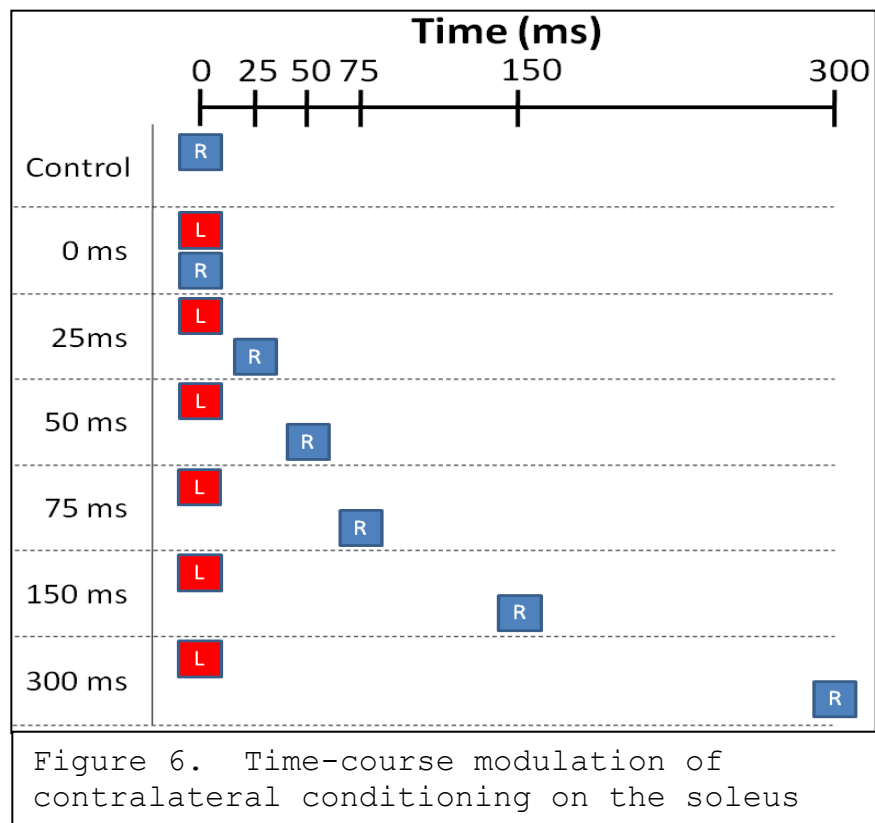
Experimental Protocol

After the electrode placement, subjects were asked to lie in the supine position on an examining table (Figure 5). Before testing started, each subject was tested to find their maximal motor and H-reflex responses (Mmax and Hmax, respectfully) and 50% of their Hmax in the right leg, which was used as the control H-reflex intensity.



A 1 ms square wave pulse was used to stimulate the posterior tibia nerve of the right leg and elicit the H-reflex. For the left leg common peroneal nerve, a 1 ms square pulse was used to evoke a motor response. The intensity for the common peroneal stimulation was set to 1.2x motor threshold. A series of 15 control H-reflexes were elicited at 50% of the Hmax prior to the conditioning paradigm. The conditioning-testing paradigm was as follows: to assess crossed-spinal reflex modulation a conditioning stimulus was delivered to the common peroneal nerve of the left leg using a 160 Hz train, 20 ms in duration, at 1.2x motor threshold. This conditioning stimulus was followed by stimulation of the posterior tibial nerve of the right leg, which produced an H-reflex. An interval of 10 seconds was used

between each trial to reduce any potential homosynaptic depression effects. This study used a series of conditioning intervals (0ms/control, 25ms, 50ms, 75ms, 150ms, and 300ms), which were used to assess the time-course modulation of contralateral conditioning on the soleus H-reflex. This conditioning protocol is illustrated in Figure 6.



Each of the six conditioning intervals were tested 10 times, resulting in 60 conditioned H-reflexes responses. The conditioning intervals were chosen based on literature that demonstrated the amount of inhibition or excitation in the test reflex is dependent on the conditioning-test interval and that

modulation in the reflex can be seen across a wide range of conditioning intervals (Koceja & Kamen, 1992).

Once all 60 conditioning intervals were obtained in the supine position, each subject was then tested in an upright, weight bearing position on a force platform. The electrode placement along with the stimulus intensities and conditioning-test intervals were all preserved from supine to standing. To prevent standing subjects from falling, a Biodex® body support system will be used. The Biodex® body support system was used, in the event of loss of balance, to support the subject's entire weight, not allowing him/her to fall to the ground. Total experimental time for each subject was approximately 1 hour and 30 minutes. A custom Matlab® (MathWorks, Inc.) was used to randomly assign subjects to a conditioning interval order for both standing and supine.

Chapter 4

Results

In this chapter, results will be presented in the following order: 1) Subjects demographics; 2) H-reflex modulation; and 3) Summary.

Subject Demographics

Subjects were recruited through their personal physician or physical therapist. We tested 4 high-risk fallers. The average age of the subjects was 72.65 ± 5.22 years. All subjects had a history of falling, as determined by personal physician or physical therapist.

H-reflex Modulation

All H-reflex measurements were elicited in supine and standing conditions for all subjects with the exception of one subject who could not tolerate being placed in supine position. Ten H-reflexes were acquired at each of the following interstimulus intervals: 0ms (control), 25ms, 50ms, 75ms, 150ms, and 300ms. Individual subject's H-reflexes were pooled for each interstimulus interval and averaged. The differences between standing and supine conditioned H-reflex facilitation is

presented in Figure 7. Conditioned H-reflex amplitudes are presented as a percent of control (unconditioned).

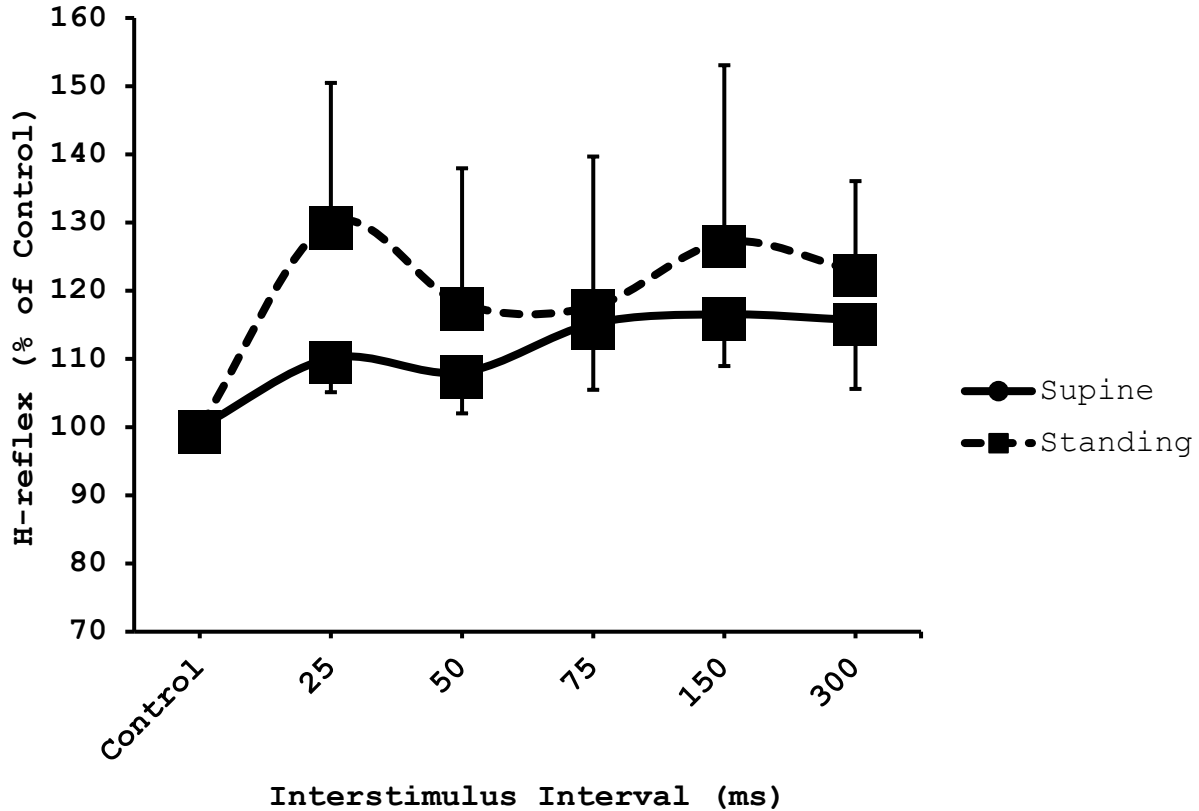


Figure 7. Percentage of soleus H-reflex facilitation in high-risk fallers. No significant differences were found. However, at 25ms and 150ms there was a trend toward significance. Error bars represent standard error of the mean.

A 2 x 6 ANOVA (body position x interval) revealed no significance interaction $F_{(5, 15)} = 0.23$, $p = 0.93$. Similarly there was no significant main effect for body position $F_{(1, 15)} = 0.178$, $p = 0.702$ or interval $F_{(5, 15)} = 01.29$, $p = 0.319$. When examining the ISIs of 25ms and 150ms, there was 129.9% increase in the

conditioned H-reflex response when standing and a 110.1% increase when supine at 25ms; similarly at the 150ms there was also considerably more facilitation when standing (127.13% vs 116.53%). Although not significant, most likely due to the small sample size, the general trend at these intervals indicated subjects had greater facilitation of their conditioned H-reflex response when standing compared to supine (Figure 8).

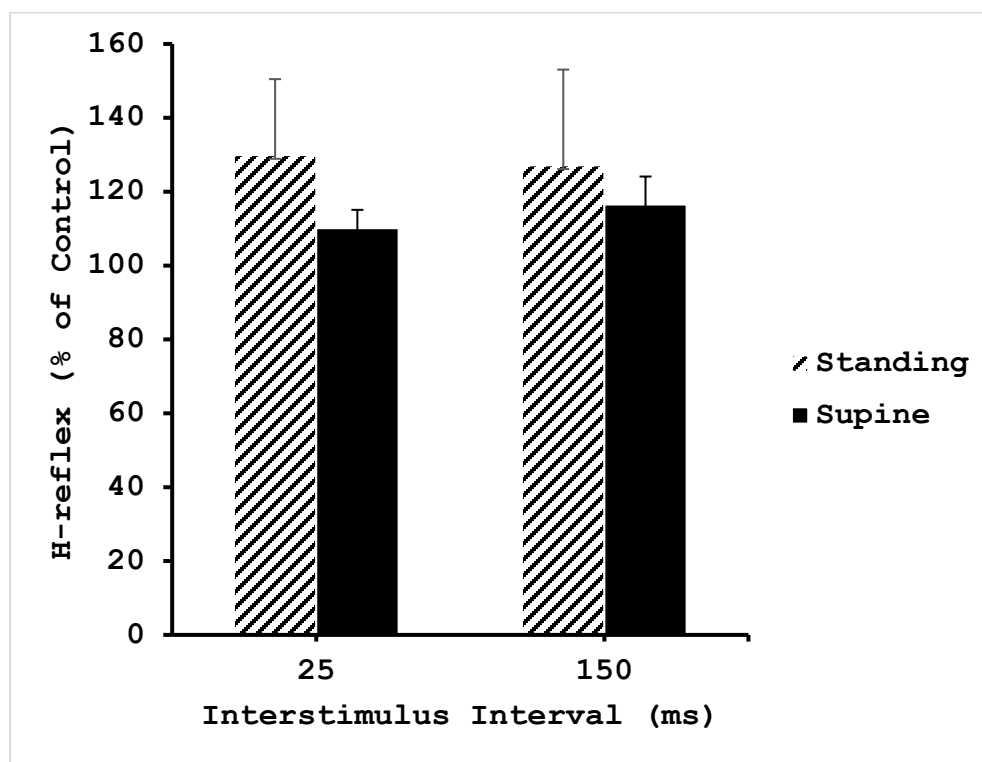


Figure 8. Percentage of soleus H-reflex facilitation at 25ms and 150ms interstimulus intervals for supine and standing conditions. While no significance was found at these ISIs, this figure depicts a trend of greater facilitation when standing. Error bars represent standard error of the mean.

Given the lack of significance, and the small sample size, a post hoc power analysis was conducted using G-Power. This analysis indicated that approximately 8-14 subjects were needed to detect significant differences in reflex modulation in high-risk fallers at the 0.05 level of significance. It is recommended that this study be replicated in an environment in which greater access to high-risk individuals is possible.

Chapter 5

Discussion, Conclusion and Recommendations

This chapter will be used for interpretation of the results presented in the previous chapter and the significance of the results with regard to and in light of previous research.

Discussion

This study examined the role of body position in conditioning the soleus H-reflex with a stimulus train from the contralateral common peroneal nerve in a group of high-risk fallers. The results of this study did not reveal significant differences in the modulation of the soleus H-reflex following conditioning stimuli to the contralateral common peroneal nerve. Despite a lack of power to detect significance at the 0.05 level, two potential areas of interest emerged: 1) at the 25 ms interval, the high-risk fallers demonstrated facilitation of the conditioning effect of the soleus H-reflex of 129.9% standing versus 110.1% supine; and 2) at 150 ms interval the high-risk fallers again showed greater facilitation of the conditioned soleus H-reflex when weight-bearing (127.13% standing versus 116.53% supine). These results differ from what is expected in a young, healthy population, but fit into one of two groups of older adults. Koceja et al., (1993) demonstrated that young, healthy subjects suppress the H-reflex response when moving from

a prone to standing position, while older adults fall in two groups with regard to H-reflex modulation and body position: 1) those that depress the reflex in a similar way to young subjects; and 2) those that do not depress the H-reflex. Further, this study also demonstrated that those elderly subjects who were unable to suppress the reflex pathways when standing were also more unstable in their standing posture. A similar trend was observed in this study: the high-risk fallers demonstrated greater facilitation (although not statistically significant) when standing.

Further differences between the results of this study and previous studies can be seen when examining the conditioned soleus H-reflex response to non-weight bearing conditions alone. Several studies using soleus EMG responses (P.W. Stubbs & Mrachacz-Kersting, 2009), soleus H-reflex responses (Stubbs et al., 2011), and patellar tendon reflexes (Kamen & Kocaja, 1989) have found a slight inhibition of the conditioned response at the 25ms ISI. High-risk fallers from this study, however, showed no such inhibition at the 25ms ISI; contrariwise, the high-risk fallers examined for this study showed only facilitation of the conditioned soleus H-reflex at the 25ms ISI and all other ISIs tested.

The lack of proper modulation of the conditioned soleus H-reflex when moving from a standing to supine position in high-risk fallers along with a lack of inhibition the soleus H-reflex response when supine at the 25ms ISI suggests that this group of high-risk fallers has an inability to appropriately modulate crossed-spinal reflexes in accordance with their environment. At short ISIs, such as 25ms, the initial ability to maintain a proper reflex response following a perturbation is completely reliant on the integrity of spinal circuits as supraspinal input takes approximately 75ms-100ms to reach the soleus muscle. Given that our data suggests inappropriate modulation of the soleus H-reflex following a perturbation in high-risk fallers, it is possible that this lack of proper modulation is an underlying reason for their past histories of falls.

Summary and Conclusion

When the contralateral soleus H-reflex was conditioned, high-risk fallers showed a facilitation of the reflex when moving from a supine to standing position. While this study lacked enough subjects to produce the power necessary to show significance at the 0.05 level, the trend suggests that at the ISIs of 25ms and 150ms there is a greater amount of facilitation when standing. This inappropriate modulation of the reflex could have potentially contributed to their past histories of falls.

Future Recommendations

Greater focus needs to be put on subject recruitment. With so few subjects taking part in this study, there was not enough power to detect significant differences. Additionally, with the difficulties in recruiting the four subjects we had, this study's inclusion criteria had to be expanded. In future studies with an appropriate number of subjects, the inclusion criteria should be stricter to rule out any confounding conditions that could have attributed to differences and classification as a "high-risk faller." Additionally, adding another measurement of stability such as Tinetti or postural sway scores, in addition to the H-reflex conditioning results, could provide a more complete picture of the contributing components that have resulted in past falls. If fruitful, these variables may help in identifying members of the population that are at an increased risk for falls.

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Appendix

Appendix A

Questionnaire

- 1- How old are you?
- 2- Have you been diagnosed with any neurological problem (Has your doctor or healthcare provider told you that you have had stroke, MS, ALS, peripheral neuropathy or similar diseases)?
- 3- Can you stand independently or with the aid of an assistive device (such as a cane) for 5 minutes?
- 4- Can you walk independently or with the aid of an assistive device (such as a cane) for 5 minutes?
- 5- Do you have any sensory problem or movement problem in the non-affected side (for example, you cannot feel cold or hot water with your unaffected hand)?
- 6- Do you have any problem with speaking? Has your doctor or health care provider told you that you have aphasia?
- 7- Do you suffer from uncontrolled high blood pressure?
- 8- Did you have any heart problems during the past 12 months (such as myocardial infarction, congestive heart failure)?
- 9- If you walk for 10 minutes, will you develop pain and discomfort in your lower limbs? Has your doctor or health care provider told you that you have *intermittent claudication*?

Appendix B

IRB approval # 1310638125